Amendments to the Claims

Claims:

The current status of all claims is listed below and supercedes all previous lists of claims.

Please cancel pending claims 15-18, 20-25, 28-36, 38-41, 44-46, 53-54, 56-57, 60-62, 64-68, 70-71 and 73-74 without prejudice to the applicants' right to reinstate those claims or pursue them in a further application.

Please amend claims 3-5, 7, 9, 11-13, 26 and 42, as follows (deleted text is shown in strike-through font, and new text is underlined).

1. (original) A method for detecting a cancer cell in a subject, said method comprising determining the level of nucleic acid that is linked to map position 8q22.3 of the human genome or an expression product thereof in a sample of said subject, wherein an elevated level of said nucleic acid or said polypeptide is indicative of cancer in the subject.

2. (original) The method according to claim 1 wherein the cancer cell is epithelial in origin.

3. (currently amended) The method ~~according to~~ of claim 1 ~~or claim 2~~ wherein the cancer cell is from a cancer selected from the group consisting of ovarian cancer, melanoma, metastatic melanoma, squamous cell carcinoma of the head and neck, squamous cell carcinoma of the tongue, hepatocellular carcinoma, breast cancer, a metastases of ovarian cancer, a metastases of melanoma, a metastases of metastatic melanoma, a metastases of squamous cell carcinoma of the head and neck, a metastases of squamous cell carcinoma of the tongue, a metastases of hepatocellular carcinoma and a metastases of breast cancer.

4. (currently amended) The method ~~according to any one~~ of ~~claims~~ claim 1 ~~to 3~~ wherein the nucleic acid that is linked to map position 8q22.3 of the human genome comprises the genomic *Edd* and *p53R2* genes or a portion thereof.

5. (currently amended) The method ~~according to any one~~ of ~~claims~~ claim 1 ~~to 4~~ wherein the nucleic acid that is linked to map position 8q22.3 of the human genome comprises a genomic gene encoding an EDD protein.

6. (original) The method of claim 5 wherein the EDD protein is a polypeptide that comprises an amino acid sequence having at least 80% identity to the sequence set forth in SEQ ID Nos: 2 or 4.

7. (currently amended) The method of ~~any one of claims~~ claim 1 ~~to 6~~, said method comprising:

(i) determining the level of nucleic acid linked to map position 8q22.3 of the human genome in a test sample from said subject; and

(ii) comparing the level of the nucleic acid at (i) to the level of the nucleic acid in a reference sample from a healthy or normal individual,

wherein a level of the nucleic acid at (ii) that is enhanced in the test sample relative to the reference sample from the normal or healthy individual is indicative of the presence of a cancer cell in said subject.

8. (original) The method of claim 7 wherein the test sample and the reference sample comprise a cell from a tissue selected from the group consisting of skin, an oral cavity tissue, breast, liver, spleen, ovary, prostate, kidney, uterus, placenta, cervix, omentum, rectum, brain, bone, lung, lymph, urine, semen, blood, abdominal fluid, and serum.

9. (currently amended) The method of ~~any one of claims~~ claim 1 ~~to 8~~ wherein the level of nucleic acid linked to map position 8q22.3 of the human genome is determined by hybridizing a nucleic acid probe to genomic DNA encoding an EDD protein in the sample under stringency hybridization conditions and detecting the hybridization using a detection means.

10. (original) The method of claim 9 wherein the detection means is nucleic acid hybridization or amplification reaction.

11. (currently amended) The method of ~~any one of claims~~ claim 1 ~~to 10~~ wherein the level of nucleic acid that is linked to map position 8q22.3 of the human genome is determined by hybridizing a nucleic acid probe or primer to genomic DNA and detecting the hybridization, wherein the probe or primer comprises a nucleotide sequence selected from the group consisting of:

(i) the sequence set forth in SEQ ID NO: 5;

(ii) the sequence set forth in SEQ ID NO: 6;

(iii) the sequence set forth in SEQ ID NO: 7;

(iv) the sequence set forth in SEQ ID NO: 24;

(v) the sequence set forth in SEQ ID NO: 25; and

(vi) the sequence of a nucleic acid fragment produced by amplification using any one of (i) to (v) as amplification primers in PCR.

12. (currently amended) The method of ~~any one of claims~~ claim 1 ~~to 11~~ wherein the sample has been obtained previously from the subject.

13. (currently amended) The method of ~~any one of claims~~ claim 1 ~~to 10~~ wherein the level of nucleic acid that is linked to map position 8q22.3 of the human genome is determined by hybridizing a nucleic acid probe or primer to genomic DNA and detecting the hybridization, wherein the probe or primer comprises a nucleotide sequence selected from the group consisting of:

(i) the sequence set forth in SEQ ID NO: 3;

(ii) the sequence set forth in SEQ ID NO: 5;

(iii) the sequence set forth in SEQ ID NO: 6;

(iv) the sequence set forth in SEQ ID NO: 7;

(v) the sequence set forth in SEQ ID NO: 24;

(vi) the sequence set forth in SEQ ID NO: 25;

(vii) the sequence of a nucleic acid fragment produced by amplification using ~~(vi)~~ (v) and ~~(vii)~~ (vi) as amplification primers in PCR;

(viii) the sequence set forth in SEQ ID NO:26;

(ix) the sequence set forth in SEQ ID NO: 27;

(x) the sequence of a nucleic acid fragment produced by amplification using ~~(ix)~~ (viii) and ~~(x)~~ (ix) as amplification primers in PCR;

(xi) the sequence set forth in SEQ ID NO: 28;

(xii) the sequence set forth in SEQ ID NO: 29;

(xiii) the sequence set forth in SEQ ID NO: 30;

(xiv) the sequence of a nucleic acid fragment produced by amplification using (xii) and (xiii) as amplification primers in PCR;

(xv) the sequence set forth in SEQ ID NO: 33;

(xvi) the sequence set forth in SEQ ID NO: 34;

(xvii) the sequence of a nucleic acid fragment produced by amplification using (xv) and (xvi) as amplification primers in PCR;

(xviii) the sequence set forth in SEQ ID NO: 37;

(xix) the sequence set forth in SEQ ID NO: 38;

(xx) the sequence of a nucleic acid fragment produced by amplification using (xvii) and (xix) as amplification primers in PCR;

(xxi) the sequence set forth in SEQ ID NO: 40; and

(xxii) a sequence that is complementary to any one of (i) to (xxi).

14. (original) A method for detecting a cancer cell in a subject, said method comprising:

(i) determining the level of mRNA encoded by nucleic acid linked to map position 8q22.3 of the human genome that is expressed in a test sample from said subject; and

(ii) comparing the level of the mRNA determined at (i) to the level of mRNA encoded by nucleic acid linked to map position 8q22.3 of the human genome that is expressed in a reference sample from a healthy or normal individual,

wherein a level of the mRNA at (i) that is enhanced in the test sample relative to the reference sample from the normal or healthy individual is indicative of the presence of a cancer cell in said subject.

15-18. (cancelled)

19. (original) A method for diagnosing a cancer or predicting recurrence of a cancer in a subject comprising determining the level of mRNA or protein encoded by nucleic acid linked to map position 8q22.3 of the human genome in a sample of said subject, wherein an elevated level of said mRNA or protein is indicative of relapse of a cancer in said subject.

20-25. (cancelled)

26. (currently amended) An isolated nucleic acid molecule for detecting a cancer cell comprising a nucleotide sequence selected from the group consisting of:

(i) a sequence that encodes the amino acid sequence set forth in SEQ ID NO: 4 wherein said amino acid sequence lacks the sequence VLLLPL;

~~(i)~~ (ii) the sequence set forth in SEQ ID NO: 3;

~~(ii)~~ (iii) the sequence set forth in SEQ ID NO: 5;

~~(iii)~~ (iv) the sequence set forth in SEQ ID NO: 6;

~~(iv)~~ (v) the sequence set forth in SEQ ID NO: 7;

~~(v)~~ (vi) the sequence set forth in SEQ ID NO: 24;

~~(vi)~~ (vii) the sequence set forth in SEQ ID NO: 25;

~~(vii)~~ (viii) the sequence of a nucleic acid fragment produced by amplification using (vi) and (vii) as amplification primers in PCR;

~~(viii)~~ (ix) the sequence set forth in SEQ ID NO:26;

~~(ix)~~ (x) the sequence set forth in SEQ ID NO: 27;

~~(x)~~ (xi) the sequence of a nucleic acid fragment produced by amplification using (ix) and (x) as amplification primers in PCR;

~~(xi)~~ (xii) the sequence set forth in SEQ ID NO: 28;

~~(xii)~~ (xiii) the sequence set forth in SEQ ID NO: 29;

~~(xiii)~~ (xiv) the sequence set forth in SEQ ID NO: 30;

~~(xiv)~~ (xv) the sequence of a nucleic acid fragment produced by amplification using ~~(xii)~~ (xiii) and ~~(xiii)~~ (xiv) as amplification primers in PCR;

~~(xv)~~ (xvi) the sequence set forth in SEQ ID NO: 33;

~~(xvi)~~ (xvii) the sequence set forth in SEQ ID NO: 34;

~~(xvii)~~ (xviii) the sequence of a nucleic acid fragment produced by amplification using ~~(xv)~~ (xvi) and ~~(xvi)~~ (xvii) as amplification primers in PCR;

(~~viii~~) (xix) the sequence set forth in SEQ ID NO: 37;

(~~ix~~) (xx) the sequence set forth in SEQ ID NO: 38;

(~~xx~~) (xxi) the sequence of a nucleic acid fragment produced by amplification using (~~xviii~~) (xix) and (~~ix~~) (xx) as amplification primers in PCR;

(~~xxi~~) (xxii) the sequence set forth in SEQ ID NO: 40; and

(~~xxii~~) (xxiii) a sequence that is complementary to any one of (i) to (xxi).

27. (original) An isolated or recombinant protein complex comprising:

(i) an EDD protein or a portion of an EDD protein sufficient to bind to a protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein; and

(ii) a nuclear protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein and a progesterone receptor protein or a portion of said protein sufficient to bind to said EDD protein or said portion of an EDD protein.

28-36. (cancelled)

37. (original) An isolated antibody that binds to a protein complex comprising an EDD protein.

38-41. (cancelled)

42. (currently amended) An isolated antibody that binds to the antibody of ~~any one of claims~~ claim 3 ~~to 41~~.

43. (original) A kit for detecting or producing a protein complex, said kit comprising an EDD polypeptide or a portion of an EDD polypeptide and a second polypeptides selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or

damage, a nuclear targeting protein, and a progesterone receptor protein or a portion thereof, wherein the portion of the second polypeptide is sufficient to bind to said EDD polypeptide or said portion of an EDD polypeptide.

44-46. (cancelled)

47. (original) A kit for detecting or producing a protein complex comprising:

(i) a first compartment comprising an EDD protein or a portion thereof sufficient to form a protein complex selected from the group consisting of: a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein or a portion thereof, wherein the portion of the second polypeptide is sufficient to bind to said EDD polypeptide or said portion of an EDD polypeptide; and

(ii) a second compartment comprising an antibody or ligand that binds to a protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein or a portion thereof.

wherein said antibody or ligand that binds to a protein complex does not bind to the individual protein binding partners.

48. (original) A kit for detecting or producing a protein complex comprising:

(i) a first compartment comprising an EDD protein or a portion thereof sufficient to form a protein complex selected from the group consisting of: (i) a complex comprising EDD and CHK2; (ii) a complex comprising EDD and BRCA2; (iii) a complex comprising EDD and CIB; (iv) a complex comprising EDD and importin alpha-1; (v) a complex comprising EDD and importin alpha-3; (vi) a complex comprising EDD and importin alpha-5; and (vii) a complex comprising EDD and progesterone receptor; and

(ii) a second compartment comprising an antibody or ligand that binds to a protein selected from the group consisting of (i) a CHK2 protein; (ii) a BRCA2 protein; (iii) a CIBCIB protein; (iv) an importin alpha-1 protein; (v) an

importin alpha-3 protein; (vi) an importin alpha-5 protein; and (vii) a progesterone receptor protein, or an antibody or ligand that binds to a protein complex selected from the group consisting of: (i) a complex comprising EDD and CHK2; (ii) a complex comprising EDD and BRCA2; (iii) a complex comprising EDD and CIB; (iv) a complex comprising EDD and importin alpha-1; (v) a complex comprising EDD and importin alpha-3; (vi) a complex comprising EDD and importin alpha-5; and (vii) a complex comprising EDD and progesterone receptor.

wherein said antibody or ligand that binds to a protein complex does not bind to the individual protein binding partners.

49. (original) A kit for detecting or producing a protein complex comprising:

(i) a first compartment comprising an antibody or ligand that binds to an EDD protein; and

(ii) a second compartment comprising a protein selected from the group consisting of (i) a CHK2 protein; (ii) a BRCA2 protein; (iii) a CIB protein; (iv) an importin alpha-1 protein; (v) an importin alpha-3 protein; (vi) an importin alpha-5 protein; and (vii) a progesterone receptor protein, or a portion thereof sufficient to bind to an EDD protein.

50. (original) A kit for detecting or producing a protein complex comprising:

(i) a first compartment comprising an isolated or recombinant protein complex selected from the group consisting of: (i) a complex comprising EDD and CHK2; (ii) a complex comprising EDD and BRCA2; (iii) a complex comprising EDD and CIB; (iv) a complex comprising EDD and importin alpha-1; (v) a complex comprising EDD and importin alpha-3; (vi) a complex comprising EDD and importin alpha-5; and (vii) a complex comprising EDD and progesterone receptor; and

(ii) a second compartment comprising an (i) antibody or ligand that binds to a polypeptide selected from the group consisting of a CHK2 protein, a BRCA2 protein, a CIB protein, an importin alpha-1 protein, an importin alpha-3 protein, an importin alpha-5 protein, a progesterone receptor protein and an

EDD protein; or (ii) an antibody or ligand that binds to one or more protein complexes (a).

51. (original) A method for isolating a protein complex comprising an EDD protein or a protein of an EDD protein and a protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein from a suitable cellular source, said method comprising contacting an extract of said cell with an EDD polypeptide or a portion thereof that binds to said protein for a time and under conditions sufficient for a protein complex to form and then isolating the protein complex formed.

52. (original) A method of isolating the protein complex comprising an EDD protein or a protein of an EDD protein and a protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein comprising:

(i) isolating a protein that is a component of the protein complex from a cell that expresses said protein;

(ii) isolating another protein that is a component of the protein complex from a cell that expresses said other protein; and

combining the proteins isolated at (i) and (ii) in an amount and under conditions sufficient to facilitate the formation of a protein complex.

53-54. (cancelled)

55. (original) A method for determining a predisposition for disease, or a disease state, said method comprising detecting a protein complex comprising:

(i) an EDD protein; and

(ii) a protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, a progesterone receptor protein and a protein associated with vascularization,

wherein an elevated level of said protein complex is indicative of a predisposition for disease, or a disease state in said subject.

56-57. (cancelled)

58. (original) A method for determining a modulator of the activity, formation or stability of an isolated or recombinant protein complex comprising:

(i) determining the activity, formation or stability of a protein complex comprising (a) an EDD protein or a portion of an EDD protein; and (b) a protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein or a portion thereof, wherein the portion of the second polypeptide is sufficient to bind to said EDD polypeptide or said portion of an EDD polypeptide, in the absence of a candidate compound or candidate antibody; and

(ii) determining the level of said protein complex in the presence of a candidate compound or in the presence of said candidate antibody

wherein a difference in the level of said protein complex at (i) and (ii) indicates that the candidate compound or candidate antibody is a modulator of said interaction.

59. (original) A method for determining a modulator of the level of protein complex formation comprising:

(i) determining the level of a protein complex comprising (a) an EDD protein or a portion of an EDD protein; and (b) a protein selected from the group consisting of a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein or a portion thereof, wherein the portion of the second polypeptide is sufficient to bind to said EDD polypeptide or said portion of an EDD polypeptide, in the absence of a candidate compound or candidate antibody; and

(ii) determining the level of said protein complex in the presence of a candidate compound or in the presence of said candidate antibody

wherein a difference in the level of said protein complex at (i) and (ii) indicates that the candidate compound or candidate antibody is a modulator of said interaction.

60-62. (cancelled)

63. (original) A method for treating a condition associated with elevated expression of an EDD protein in a cell, said method comprising administering an amount of a compound effective to reduce EDD expression in a cell.

64-68. (cancelled)

69. (original) An antisense nucleic acid, ribozyme, PNA, interfering RNA or siRNA comprising a sequence having at least 80% homology to SEQ ID NO: 47.

70-71. (cancelled)

72. (original) A pharmaceutical composition comprising the antisense nucleic acid, ribozyme, PNA, interfering RNA or siRNA of claim 69.

73-74. (cancelled)

75. (original) A method for determining the ability of a cell to phosphorylate CHK2 in response to a DNA damaging agent comprising determining the level of expression of EDD in said cell, wherein reduced or suppressed EDD expression indicates that the cell has reduced ability to phosphorylate CHK2 in response to a DNA damaging agent.